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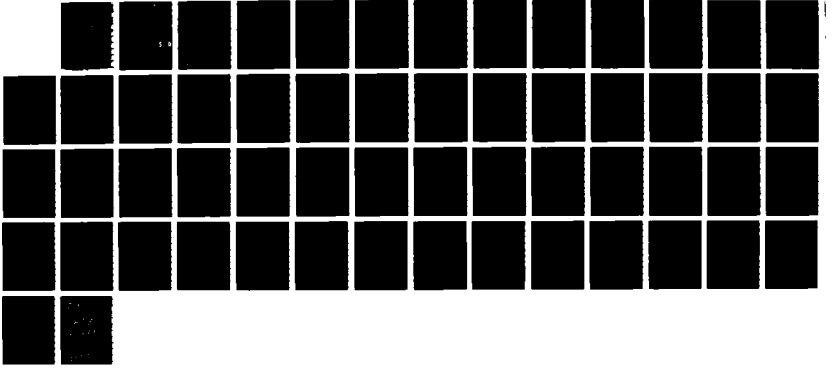

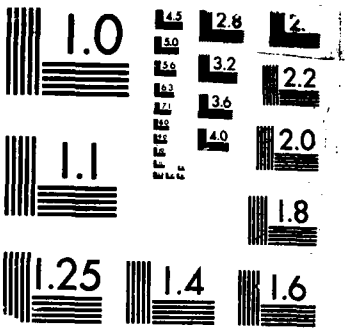

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PATTERN RECOGNITION OF CARDIOVASCULAR AND PSYCHOMOTOR VARIABILITY IN RESPONSE TO PHARMACOLOGICAL AGENT

Annual Report

Murray H. Loew, Ph.D.

June 10, 1985

Supported by

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1. INTRODUCTION

This is the first in a series of annual reports submitted by George Washington University in partial fulfillment of the requirements of U.S. Army Contract No. DAMD 17-84-C-4129, entitled, "Pattern Recognition of Cardio-Vascular and Psychomotor Variability in Response to Pharmacological Agent." The goal of the work is to develop pattern-recognition and signal-processing methods that will use Army-supplied human cardiovascular and psychomotor data to provide indices of responsivity to challenge. Time Series and point-process techniques will form the basis of the approach, and the assumptions that underlie the methods will be examined and tested. The detection of infrequent and brief events, and the elucidation of their relationships, if any, to the indices, will be carried out.

This report describes the work over the past year that has provided a background--principally physiological--for the detailed analysis that is expected in Year 2.

2. BACKGROUND AND WORK TO DATE

2.1 Physiology

This section is composed of three subsections. The first contains a review of recent literature dealing with heart rate

and its origins, including sources of variability. Measures of activity are also discussed briefly.

Clearly, it is important in an analysis of this kind to account for known factors that can influence heart rate (HR) or its variability (HRV). The risk is thereby reduced that incorrect weighting will be given to some of the components of HRV, or to HR itself, in the estimation of performance or readiness measures. Specifically, we wish to consider the effects of respiration, drugs, activity, circadian and other rhythms, and sleep deprivation on HR and HRV.

The second subsection is an annotated bibliography that extracts and summarized the salient points of a set of relevant papers, and also provides commentary where especially important or questionable statements appear.

The third subsection consists of a list of references, found as part of an automated literature search, that has been arranged according to apparant priority of importance to this work. They will be investigated and added to the annotated set during the next year.

2.1.1 Report on Relevant Physiology

2.1.1.1 Physiology of the Heart

The heart initiates its own contraction in the sinoatrial (S-A) node, the primary pacemaker, but controlling centers in the

brain and spinal cord alter the time between firings as well as the time for one cardiac cycle. Messages from these centers are transmitted by means of the autonomic system which is subdivided into parasympathetic (vagal) and sympathetic outflows.

What causes the heart to beat is the spontaneous depolarization of the S-A node pacemaker cells followed by the spread of electricity across the heart along several preferred pathways in the interatrial septum and Bachman's bundle, triggering the depolarization and repolarization of the rest of the cells. This electrical activity can be seen in the electrocardiogram (ECG). The individual cells of the heart gain and lose action potential during the polarization, depolarization and subsequent repolarization which is the source of the current measured by the ECG. In other words, an ECG is proportional to the summed action potential of all cells.

Fig.1 shows the standard view of the deflections of an ECG. The P wave represents atrial depolarization. The PR interval is a measure of the time it takes the impulse to travel between the sinus node and the inception of the bundle branches. It includes a delay at the AV node. The QRS complex is produced by the spread of electricity through the ventricular myocardium. The ST interval is a brief period of minimal electrical activity following ventricular depolarization. The T wave represents ventricular repolarization.

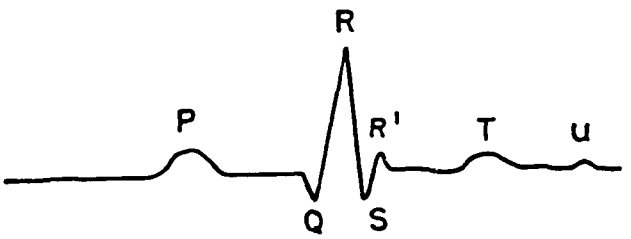

Figure 1 Electrocardiogram Deflection

Rahr, et. al. [1984] characterize normal sinus rhythm as a regular rhythm with 60 to 100 beats per minute, cycle length varying not more than 10%, and P waves having normal contours. Sinus tachycardia, found in both healthy and diseased states, is characterized by regular rhythm and more than 100 beats per minute. Sinus Bradycardia has slower than normal but still regular rhythm.

McDonald [1980, p.4] points out that the heart rate depends on the slope of diastolic depolarization which is altered by the autonomic nervous system. The automatic system reaches all parts of the heart although "...the precise distribution of either sympathetic or parasympathetic terminations around effector cardiac cells remains unknown" (Randall, 1984, pp.47-48). However, one of the densest areas of innervation is found in the S-A node.

The autonomic system influences the rate of depolarization of the S-A node by the release of autonomic transmitters. The autonomic transmitter released by the parasympathetic nervous system is acetylcholine which interacts with muscarinic receptors in the heart. Norepinephrine, released by sympathetic nerves, interacts with the adrenergic receptors which are of 2 types, either alpha or beta. These transmitters influence the permeability of the cell membrane to the flow of potassium and sodium ions.

At the receptor level, cardiac control is very complex. Neurotransmitter receptors themselves are subject to regulation in a variety of ways and their numbers do not remain fixed over time. For example, adrenergic receptors are affected not only by norepinephrine released from sympathetic nerves but also by catecholamines diffused from the bloodstream. "Also, the sympathetic system itself appears to be regulated by 'presynaptic' receptors which either inhibit or facilitate transmitter release" (Wikberg, Lefkowitz, 1984, p.95).

The heart responds to parasympathetic action by decreasing its rate of contraction, depressing or blocking A-V conductivity, and decreasing the force of both atrial and ventricular contraction. In addition, the atrial refractory period is shortened. The effect on the ventricular refractory period is not clear, however. Sympathetic action produces an opposite effect: rate of contraction, A-V conduction velocity, and force of contraction all increase, as does the refractory period.

Levy and Martin [1984, p.68] report that after stimulation by the cardiac sympathetic nerves, the changes in heart rate "...tend to be slow in onset and to decay slowly upon cessation of stimulation." In contrast, the changes in heart rate caused by a stream of vagal impulses "...appear after a brief latent period, reach a steady-state response within a few beats, and decay rapidly back to the control level when stimulation is discontinued." They go on to point out that recent studies indicate that heart rate response to constant vagal stimulation does not remain at a constant level, but seems to diminish somewhat over the next several beats before a steady-state level is reached. The possible cause is receptor or effector desensitization.

Wurster [1984, p.315], agrees with their assessment of sympathetic response but states that the heart rate changes within "...a small fraction of a single cardiac cycle" under vagal regulation. The difference of opinion as to how quickly the vagal influences heart rate reflects the fact that the effect of vagal stimulation varies with respect to when in the cardiac cycle it is applied.

The role of the autonomic nervous system is to maintain a stable internal environment. There is evidence that the autonomic centers which control the sympathetic and parasympathetic outflows are located in spinal, medullary, hypothalamic, limbic, and other forebrain structures. Wurster [1984, p.307] describes the central nervous system structures that deal with cardio-

vascular control as multilevel circuits interconnecting these "centers." A lesion in one component will alter but not totally impair a function; the removal of a single component may produce a deficit only under certain conditions such as exercise or emotional stress. Modern neuroanatomical tracing techniques have shown these circuits to be very complex.

Current views of autonomic control of the cardiovascular system show the system to be more complicated than previously believed. First of all, parasympathetic and sympathetic outflows which were thought to behave only in a reciprocal fashion, are now thought to act either reciprocally or separately, increasing or decreasing simultaneously (Wurster, 1984, p.310). McDonald [1980, pp. 6-7] reports similar findings, pointing out that "...cardiac slowing, induced by an acute rise in arterial pressure, is due to increased vagal activity, inhibition of the sympathetic having no important effect. Conversely, cardiac acceleration caused by a fall in blood-pressure is mediated by an increase in sympathetic activity rather than by vagal withdrawal." Moreover, complex interactions occur when both the sympathetic and parasympathetic nerves are active at the same time. The principal interaction is called "accentuated antagonism." "Under its influence the inhibitory effect of a given level of vagal activity becomes more pronounced the greater the prevailing level of sympathetic activity" (Levy, Martin, 1984, p.84).

Secondly as Wurster [1984, p.310] reports, the sympathetic nervous system "...was thought to affect virtually all cardiovascular effectors in a similar manner under principally emergency circumstances." Now, however, it is recognized that "...separate outputs to individual cardiovascular effectors, e.g. heart and a particular vascular bed, depend on the particular physiological state." Moreover, what is proposed is that outflows may be specific to a particular effector organ or subsystem of, for example, the cardiovascular system, or "...more than one control circuit may utilize the same pathway for regulation of a number of effector organs" (Wurster, 1984, pp.311-312).

The autonomic centers receive information from various receptors in order to regulate coronary blood flow. One, the baroreceptor, is a sensory nerve terminal that responds to changes in pressure. Others are chemoreceptors which detect, in the case of the cardiovascular system, the lack of CO_2 in the blood, cardiac reflexes whose role is uncertain (McDonald, 1980, p.8), and respiratory sinus arrhythmia (RSA), whose mechanism is currently under study. In addition, emotional factors, pain, and other sensations influence the regulation of outflow. These messages are sent to the centers along ingoing fibres probably located in both parasympathetic and sympathetic nerves. Adjustments to parasympathetic and sympathetic outflow to the heart and other organs follow.

Therefore, one possible cause of heart rate variability is the change in environment or psychological state which is mediated through alteration of the autonomic system. Randall and Smith [1984, p.401] state, "Heart rate changes observed during transitions from one behavioral state to another are controlled exclusively by the autonomic nervous system, including the catecholamine secretions of the adrenal gland...." The fact that emotional state can affect the cardiovascular system is noted by Vatner [1984, p.414]: "...substantial increases in heart rate and myocardial contractility occur even with the anticipation of exercise."

2.1.1.2 Respiratory Sinus Arrhythmia

RSA produces most of the variability in heart rate. What is known about RSA is that its effect on the heart does appear to be age-related. Older subjects with high resting vagal tone show little respiratory variation in heart rate while younger subjects, even with higher resting heart rates, show marked variability (McDonald 1980, p.9). The mechanism of the reflex, however, is not known. Kitney, et. al. [1982, p.414] propose a model of RSA showing it arising "...from the interaction of two nonlinear oscillatory systems, respiration and the baroreceptor loop, which exhibit the phenomenon of frequency entrainment." McDonald [1980, p.9] lists other theories such as the suggestion

that changes in intrathoracic pressure which affect cardiac filling, stimulating atrial receptors, is the main stimulus to the reflex.

RSA is the heart rate variability due to respiration. Kitney, et.al. [1982, p.141] report that the time delay between respiration and heart rate variability is about 1.5 seconds. Generally, the heart accelerates with inspiration. Wurster [1984,p.315] describes the cycle in cats as follows: "Simultaneous recordings of integrated phrenic nerve activity and the inferior cardiac nerve activity of the cat demonstrates that sympathetic nerve activity often increases before inspiration, reaching its maximum in mid to late inspiration. This activity decreases before phrenic nerve activity begins to diminish at the onset of expiration. It reaches its lowest level early in the expiratory phase and then begins to increase by mid-expiration." This cycle can vary. For example, increased arterial carbon dioxide levels cause increased sympathetic activity at inspiration, but little or no change in activity at expiration.

McCabe, et.al. [1985], from a study using cats, report that RSA is due primarily to the release of vagal tone which they demonstrate by blocking vagal influence with atrophine. McDonald [1980, p.9] draws the same conclusion.

2.1.1.3 Atropine

Atropine and related drugs are competitive antagonists of acetylcholine. The effect on the heart is complex. With large enough doses, tachydardia develops. With smaller doses, the heart rate may be slowed because it stimulates the vagal nuclei in the medulla oblongata.

Goth, in Medical Pharmacology, reports that the half-life of atropine is 13 to 38 hours, and it is excreted from the body rapidly. Fifty percent of an injected dose appears in the urine in 4 hours. The remainder is excreted within 24 hours as metabolites and the unchanged drug.

2.1.1.4. Biorhythms

Biorhythms also affect heart rate variability. For example, Orr and Hoffman [1974, p.131] propose the existence of an 80 to 100 min. periodicity in the heart rate and performance. Rhythms of other lengths also govern man's internal environment. For example, rhythms labeled circadian last about a day in length.

Examples of circadian rhythms are sleep/wakefulness, body temperature, speed of reaction, and urinary calcium excretion. These circadian rhythms average about 25 hours which means that man constantly must adjust to the 24-hour environment.

What entrains these rhythms to 24 hours are zeitgebers or time cues, the most powerful of which is the light/dark cycle. Changing the period of the zeitgebers, for example lengthening the light/dark cycle along with social cues, can force a subject into a cycle other than 24 hours. The limits of this forced environment seem to be between 23 to 27 hours (Ashoff, 1982, p.149). Outside this range, subjects will internally desynchronize.

Internal desynchronization is the state in which the phase relationships among rhythms change. In addition to occurring during forced entrainment, subjects who free-run, that is live without any time cues, will usually desynchronize within the first or second day (Kronauer, et. al., 1983, p.173).

One conclusion which can be drawn from free-running experiments is that there are 2 primary oscillators which control circadian rhythms. In desynchrony, the core body temperature rhythm can be seen to pull away from the sleep/wakefulness cycle. Other rhythms go along with one or the other.

2.1.1.5. Actigraphy

Actigraphs or actometers have been used in sleep research to predict the onset of sleep. The actigraph reported by Kripke, et.al. [1978] is a piezo-electric transducer. Its output signal was found to be a highly reliable predictor of wakefulness as determined by EEG.

In a 9-hour study of 5 normal subjects who slept at home, the actigraph measure gave highly reliable estimates of minutes of sleep, total sleep period, and the minutes of wake time within sleep. When compared with EEG estimates of the moment of sleep onset, the actigraphic estimate agreed within 2 minutes for 4 out of 5 subjects. Why activity is a good measure of sleep/wake state is explained in a conclusion they drew from many 24-hour studies which states that "...subjects moved their wrists almost continously when awake,at least once a minute, but only brief bursts of movement were seen during sleep..." (Kripke,et.al., 1978, p.674).

Other types of actigraphs have been used to measure other sorts of activity. Saris and Binkhorst studied the instrument itself and its usefulness. In their first paper [1977], they tested the reliability of their actometer which is of a different type from that of Kripke, et.al. Their actigraph measures acceleration and deceleration with a component in the same plane as the face of a watch-like instrument. They found that the reliability of individual actometers was satisfactory, but there were large differences between watches. From a study in which 6 adults and 9 children walked and ran wearing actometers on their right wrists and ankles, it was found that the actometer reacted well to intensity of movement.

In their second paper, Saris and Brinkhorst [1977] discuss how well their actometer measures daily activity. They present the results from a study of 4 kindergarten children who wore

actometers on their right ankles and wrists. The actometer measures were highly correlated to observational records prepared by the children's teachers. They concluded that the actometer is useful in studying physical activity.

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2.1.2 Annotated Bibliography

KEY

The bibliography is designed around the following outline. Only topics relevant to the type of article being reviewed are addressed. Annotation, the last topic, contains a summary of our comments about the article.

1. Topic of paper, book, or hypothesis to be tested.

2. Subjects in the experiment: how selected and how many.

3. Description of any instruments used.

4. Task.

5. Description of data collected.

6. Data analysis and statistical methods actually reported.

7. Conclusions and results. (Note: if the article is a survey, the conclusions mentioned are based on a review of the literature unless otherwise noted.)

8. Date first entered.

9. Date last revised.

10. Annotation: comments are identified by outline number.

Dr. Abramson, Pharmacology Department, GWU.

1. The following is a summary of a phone conversation in March 1985.

7. The decay function for atropine is difficult since the coefficient of the exponent of decay is a variable.

   a. The formula is:

      $c(t)=I_o e^{-kt}$

      where

      I_o=initial concentration

         k=ln2/h

         h=half life of atropine which is 13-38 hours.

   Atropine is a blocking drug, an antagonist, and the relationship between time and effect is very difficult to predict.

8. March 1985

9. March 1985

Jurgen Aschoff, *Circadian rhythms in man,* in Biological timekeeping, Cambridge University Press, 1982.

1. Chapter is an introduction to circadian rhythms in man. Book itself discusses various aspects of biological timekeeping in both plants and animals.

2. Conclusions:

   A. Man adjusted to the 24-h period of the natural environment.

   B. Man's structures and functions undergo 24-h rhythms, and the diverse rhythms maintain distinct phase relationships in an overall circadian orgnaization.

      a. Rhythms normally are coupled but can change their phase relationships and become uncoupled (i.e., free-run at different frequencies).

      b. There are a variety of rhythms: sleep/wakefulness, body temperature, alertness, composition of urine.

   C. Free-running circadian rhythms in man differ from 24-h (somewhat longer than 24-h).

   D. Problem of determining if one rhythm, say sleep/wakefulness, can "mask" rhythm of another function or if rhythm is coupled to an endogenus oscillator.

      a. Masking is used to describe what may happen when either a zeitgeber (time cue) or the sleep/wake cycle has effects on the overt state of some rhythmic physiological function but no immediate bearing on phase control of the rhythm.

      b. For example, deprivation of sleep shown to decrease amplitude of the periodic fluctuation of, for example, rectal temperature, speed of reaction, etc., indicating an endogenous oscillator. (cf. figure 9.1, p. 144).

   E. Internal temporal order (temporal order meaning phase relationship) of the free-running circadian system in man differs when entrained to 24-h.

a. Implies that various rhythms are coupled to different circadian osciallator pacemakers which can change their mutual phase relationships according to external conditions.

b. When entrained, maximum rectal temperature occurs in late afternoon and minimum during the second half of sleep. Free-running, these are advanced by several hours relative to behavioral sleep/wake cycle (cf. figure 9.4, p. 147).

F. Zeitgebers (time givers) entrain circadian rhythms. The most powerful is the light/dark cycle.

a. Artificial zeitgebers can entrain man to longer periods. Best with artificial light plus other signal like gong to indicate a specific activity (cf. p. 149). The limit seems to be 23- to 25-hour cycles for the various physiological rhythms to still change their phase relationship in a systematic order.

b. Can cause internal desynchronisation by means of a strong zeitgeber of unnatural period of longer than 27-hour. Can also happen spontaneously in free-running conditions (not yet understood).

G. Many consequences. Need to adjust for circadian rhythms when evaluating, for example, hormonal levels. Also, man responds to drugs differently in accordance with rhythms. A healthy individual shows a high degree of temporal order.

8. January 1985

9. March 1985

10. "Temporal Order" is not defined beyond the note that it includes synchronization.

Andres Goth, Medical Pharmacology, The C.V. Mosby Company, 1984.

1. The following is a summary of what was said about atropine:

7. A. It and related drugs are competitive antagonists of acetylcholine at receptor sites on organs innervated by postganglionic nerves (in smooth muscles, cardiac

muscles, and various glandular cells).

B. Acetylcholine (dictionary definition) is the chemical transmitter of the nerve impulse across a synapse and is also released by the ends of parasympathetic nerves upon stimulation; produces cardiac slowing, vasodilation, increased gastrointestinal activity, and other parasympathetic effects.

C. The effect of the competition (anatagonist vs. agonist) is greatest against the muscarinic effects of injected cholinergic drugs and against the tonic effect of the vagus nerve on the heart.

D. Atropine has less effect on the gastrointestinal tract and the bladder.

E. In low doses atropine tends to cause sedation. In larger doses, it causes stimulation which can progress to delirium then coma.

F. Therapeutic doses of 0.6 mg of atropine may cause dryness of the mouth and inhibit sweating.

G. Blockage of the cardiac vagus requires somewhat larger doses.

H. Effect of atropine on blood pressure is not impressive.

I. Effect on heart rate in humans is complex.

   a. With large enough doses, tachycardia develops.

   b. But with smaller doses, the heart rate may be slowed. Ablation experiments have shown that atropine stimulates vagal nuclei in the medulla resulting in bradycardia unless large enough doses are used to prevent such action at the muscarinic receptors.

J. Atropine causes cutaneous dilation but this effect is only partly due to its blocking sweating. Flushing of the skin may be very noticeable following moderately large doses.

K. In atropine poisoning, the CNS effects are dramatic; patients become excited, maniacal, have hot, dry skin, dilated pupils, and tachycardia.

L. Large therapeutic doses stimulate respiration and may prevent death from respiratory depression in poisoning caused by the alkylphosphate cholinesterase inhibitors.

M. Atropine is absorbed from the gastrointestinal tract and following subcutaneous injection.

N. Atropine is rapidly excreted from the body. About 50% of an injected dose appears in the urine within 4 hours. The remainder is excreted within 24 hours in the form of metabolites and the unchanged drug.

O. The duration of the pharmacological effects reflects the speed of excretion.

P. Large doses in normal people may cause unpleasant effects-- blurred vision, dry mouth, constipation, urinary retention-- but are not life-threatening.

Q. Normal individuals survive doses as high as 1 g taken by mouth.

R. The half life of atropine is 18-30 hours.

8. March 1985

9. March 1985

M. Hitchen, D.A. Brodie, and J.B. Harness, *Cardiac responses to demanding mental load,* Ergonomics, Vol. 23, 379-385, 1980.

1. Studies human responses to demanding mental work.

2. Experiment carried out on 14 healthy subjects who ranged in age from 18 to 24 years.

4. Subjects listened to a series of prerecorded digits and responded to a given odd/even sequence by pressing a switch. The task was designed to require a minimum of movement for response.

5. Data collected:

A. R peaks extracted from an ECG and interbeat interval calculated. (Article contains information on why chose

particular linear interpolation method.)

B. Peripheral blood flow information derived from data from finger plethysmograph.

C. Respiratory waveform information taken from nasal myograph data.

6. How results calculated:

A. Interbeat interval sequence displayed as a histogram at rest and during mental loading.

B. Mean heart rate--how calculated not specified.

C. Spectrum analysis on interbeat interval sequence using FFT.

a. Interpolation used: a linear interpolation method derived from control theory and a sampling frequence of 2.5 Hz was chosen. A hamming window was applied to the real and imaginary parts of the Fourier series.

7. Conclusions:

A. The histograms of the R-R interval in seconds during mental loading are less spread out and more peaked due to a decrease in heart rate variability.

B. Mean heart rate during largest mental loading increased on average by 15%.

C. In the power spectra obtained from interbeat interval, the frequency component attributed to respiration moved from approximately 0.25 Hz to 0.3 Hz during mental loading. Shift obtained in all subjects. Significance of shift or how significance calculated not reported.

D. Power spectra obtained from peripheral blood flow signal contained the same information and is therfore not needed.

E. Respiration waveform confirmed increased frequency during mental loading due to a respiratory increase, and not to other factors.

F. One subject "switched off" during most demanding test--under this test, respiratory rate started to rise but went back to level of no mental load. Responses to

test mainly incorrect. Subject did not admitto having stopped concentrating but results seem to indicate this to be the case.

8. January 1985

9. May 1985

10. (3) Does kind of mental stimulus affect response? Items (7. A, B, and D) are especially important.

Laverne C. Johnson, *Sleep Deprivation and Performance,* Biological Rhythms, Sleep, and Performance John Wiley & Sons, 1982.

1. Survey of sleep deprivation and performance research.

7. Conclusions:

   A. Some conceptual ambiguity as to completeness of sleep loss and whether total sleep loss even occurs.

      a. Idea of microsleeps.

      b. Effect of micorsleeps not established.

   B. Handling Performance Data--Lapse Hypothesis

      a. The lapse hypothesis addresses a method of handling performance data. The hypothesis says that absence of responses, not the emitted responses, is the major behavioral symptom of sleep deprivation. An earlier, alternate hypothesis measures performance by an accuracy count.

      b. Found that frequency and duration of these mental blocks increased with fatigue and that errors tended to occur at the times of these mental blocks.

      c. Present task in two ways: work-paced or self-paced.

         i. Generally, for self-paced tasks like adding, problem solving, making judgements, issuing orders, etc., speed will be impaired but accuracy will remain high.

ii. With work-paced, number of errors or missed responses significant. A subject when hit by a lapse will generally stop responding.

C. Lapse Hypothesis and Memory Impairment

a. Memory impairment occurs during sleep loss but does not fit into the lapse hypothesis as easily as impairment of vigilance and cognition. But some controversy over connection.

D. One researcher concluded that lapse hypothesis is a limited explanation of the effects of sleep loss on performance. Lowered arousal also shows itself in the subject's subjective state and as a deterioration of the capacity for sustained selective attention.

E. Also study modifier variables on sleep deprivation like fatigue and exercise. (cf. Table 1., p. 120).

a. Situational modifier factors like noise and temperature may interact with the effect of sleep loss and may explain why it is difficult to detect sleep loss effects in field studies. No evidence given.

F. Also a periodicity to effects of sleep loss.

a. Measures of performance taken at different times of the day reflect behavioral periodicity as well as increasing sleep debt.

G. Partial sleep loss both easy and difficult to define. Studies here include looking for the optimum intersleep interval necessary and how much sleep is needed for recovery. Many experiments mentioned but not cited in full.

a. Important to the military who require sustained performance in times of emergency.

8. February 1985

9. May 1985

D.F. Kripke, D.J. Mullaney, S. Messin, V.G. Wyborney, *Wrist Actigraphic Measures of Sleep and Rhythms,* Electroencephalography and Clinical Neurophysiology, Vol. 44, 674-676, 1978.

1. Describes an actigraphic telemetry system using a piezo-electric transducer and validates its usefulness in distinguishing between sleep and wakefulness.

2. A. The activity transducer consists of a small steel nut soldered off-center onto a 5-mm length of spring-like EEG pen wire, the other end of which is clamped against a piezo-ceramic element. Two resistors complete the transducer which is packaged into a small acrylic box mounted on a watch band and connected to a Medilog tape recorder. The output is a continuous analog activity recording.

   a. The voltage is not linearly related to motion or acceleration. Other specifics given.

   B. EEG recorded along with the above activity measure over 24 hour periods.

   C. What was found was that subjects move their wrists almost continuously while awake (at least once a minute), but only in brief bursts during sleep (cf. figure 2).

   D. Ran a blind independent scoring for 5 subjects (cf. Table I) of actigraphic recordings and of standard sleep recordings.

      a. Actigraphic measure was highly reliable in estimating the minutes of sleep, total sleep period, and the minutes of wake time within sleep.

      b. Actigraphic and EEG estimates of the moment of sleep onset agreed within 2 minutes for 4 out of 5 subjects.

   E. They feel that the piezo-electric transducers may be more omni-directional and more sensitive than those previously described. Apparently, previous work done with 5-minute counts rather than continous analog activity recordings.

3. April 1985

9. May 1985

Richard E. Kronauer, Charles A. Czeisler, Samuel F. Pilato, Martin C. Moore-Ede, Elliot D. Weitzman, *Mathematical Representation of the Human Circadian System: Two Interacting Oscillators Which Affect Sleep,* Sleep Disorders: Basic and Clinical Research, 1983.

1. The article does not report on the results of an experiment but presents an argument for their view of the nature of circadian oscillators. They propose a model based on two coupled oscillators.

7. A. When a subject free-runs, phase relationships among rhythms change.

    a. The phase of sleep changes (delays) significantly with respect to the core body-temperature rhythm--typically about 4 to 6 hours. Maximum body temperature is seen close to sleep onset rather than the usual two hours or so before waking. This delay can be seen in the first day or two of free-running. Also REM sleep is "more heavily weighted" to an earlier time within sleep.

    b. Gives an example from Aschoff and Wever (1976) where sleep-wake showed an average period of 29 hours while temperature cycle was 24.5 hours.

    B. Points to two oscillators, one controlling sleep-wake and the other, temperature.

    a. "The second oscillator cannot exert total control over core temperature," but the effect of second oscillator stronger.

    b. Second-oscillator hypothesis is supported by primate studies.

    C. If a coupling between the two oscillators becomes too weak or the "disparity of the periods becomes too large," the two rhythms break into their intrinsic periods. Subject now in internal desynchroniztion.

    a. Subjects vary in how long they take to desynchronize.

D. Importance of internal desynchrony to sleep research is that sleep can occur in all phases of the core temperature cycle.

   a. There seems to be a "qualitative dependence of sleep length on temperature phase"--conclusion drawn from data.

   b. "...the act of 'electing' to go to sleep (sleep onset) occurs at all phases, but not with equal probability at all phases."

E. They conclude that the oscillators are weakly nonlinear. They discuss parameters necessary to characterize the system as well as how the system works.

F. In general, the effect of the oscillator variable which dominates core temperature upon the oscillator variable which governs sleep-wake is about 4 times as strong as the effect of the sleep-wake oscillator on the core temperature oscillator.

G. For desynchrony to occur either the mutual interaction must weaken or the disparity of period between the oscillators must increase.

H. System equation given along with results of a computer simulation.

I. Something to note: the model simulations indicate that for the desynchronized subject there is a band of phases of the oscillator which dominates core temperature during which spontaneous awakening is strictly prohibited (see Figs. 10a and 10b) and another band during which spontaneous sleep onset is very unlikely. In humans, the first of these bands is one of very unlikely awakening rather than not awakening, and the other is unlikely sleep onset.

J. In general, humans have a specific rhythm generator to control sleep-wake which is unstable in its intrinsic period. A second rhythm generator that controls temperature is extremely stable in its intrinsic properties and remarkably insulated from ordinary external stiumli such as light and darkness.

K. The stable deep oscillator has a strong input to the sleep-wake one and ordinarily constrains the sleep- wake cycle time to with 4% of 24 hours. The temperature

oscillator influences the timing of sleep even if desynchrony occurs. Sleep-wake oscillator not independent.

L. The distribution of REM sleep shifts as the phase of the temperature oscillator sinusoid shifts with repsect to sleep episode. This deep oscillator important to the study of sleep dysfunction.

8. March 1985

9. May 1985

Timothy H. Monk, *Research Methods of Chronobiology,* Biological Rhythms, Sleep, and Performance John Wiley & Sons, 1982.

1. Survey of methodology.

7. The following conclusions describe the methods discussed. Few studies are cited and then only briefly. Mainly used artificial data.

A. Eyeball Technique

a. Plot whole time series and simply pick out maxima and minima.

b. Best for non-stationary series.

c. Elaboration of this technique--fit straight line to sleep onset times using least squares. Use to predict onset time for each day.

B. Buys Ballot Table

a. In circadian case, put into h x m matrix where "m" columns represent times of day and "h" rows days.

b. Average of each column represents time of day effect. A plot of this average rhythm called a chronogram or plexogram.

c. From Buys Ballot can establish goodness of fit of the rhythm--amplitude of chronogram reduced, and increase in the variance of the sample (column) used to

estimate each point of the chronogram. Cast for different periods; can plot goodness of fit to form graph called a periodogram.

C. Analysis of Variance

a. Areas of interest addressed by this approach:

i. Is there a consistent time (of day) effect?

ii. Does that effect change under manipulation X, for example, with administration of a drug.

b. Simplest design is when time is considered as a between-subject factor. Run a separate, equally matched group of subjects at each time of day being considered.

c. When time is considered as the within subject factor, each subject participates at each time of day. Problems with imporvement with practice but generally powerful. Can use latin square design to minimize learning impact.

i. Analysis of variance is conservative test of whether reliable time of day effects are present. Also weaker with more times of day--best to use two.

D. Autocorrelational Techniques

a. Examine various time lags and calculate appropriate correlation to the time series with itself for each lag. How search for predominant rhythm.

b. No assumption made about shape of underlying rhythm.

c. Requires equally spaced samples.

d. Best with comparatively long time series.

e. Can do prewhitening--smoothing by averaging adjacent points.

E. Not True Fourier Analysis--Assessment of Significance

a. Use a F ratio--sum of squared deviations about the mean divided by sum of squared deviations about the cosine curve divided by their respective degrees of

freedom. Problems with this.

b. Alternative F ratio compares the explained and unexplained sums of squares, testing the null hypothesis that the former is not greater than the latter. Also drawbacks.

c. F Ratios useful as comparative measures rather that absolute

d. Least unsatisfactory method is percentage variability. Calculated by dividing the explained sum of squares by the sum of squares about the mean and multiplying by 100.

F. Minnesota Cosinor Technique

a. Fit a single sinusoid to the time series.

b. Main dangers--using in inappropriate case when time series is non-sinusoidal, non-stationary, or insufficient in extent.

G. True Fourier Analysis

a. Can detrend by removing a linear trend in the data by fitting a straight line (by least squares) and performing all subsequent analysis on deviations from this line. Used in measures of performance efficiency where improvements due to practice can occur.

b. Tapering involves placing less emphasis of the first and last 10% of time series. Use transformation.

c. Precautions using Fourier analysis--he suggests that 200-point time series by considered minimum for computation of power spectrum. Serious problems when fewer th.n 8.0 points used.

d. Author suggests that a good check to randomly shuffle the values of time series and reapply analysis.

H. Gives chart comparing techniques.

8. February 1985

9. March 1985

10. (7.G.d.) Seems incorrect. Randomization destroys correlation properties.

Martin C. Moore-Ede *The circadian timing system in mammals in two pacemakers preside over many secondary oscillators,* Federation Proceedings, Vol. 42, No. 11, 2802-08, August 1983.

1. Presents an argument that mammals possess a major circadian pacemaker other than the known one of the suprachiasmatic nuclei (SCN) in the anterior hypothalamus. This second pacemaker is normally coupled to the SCN but can function independently. In addition, each major pacemaker presides over many secondary oscillators located in diverse tissues.

7. A. There are two main groups of endogenous circadian rhythms in humans. These rhythms can desynchronize to the extent that one group of rhythms will totally lap another, with all 360° of internal phase relationships between them observed.

B. Figure 1 shows, from the results of studies by Aschoff and Weaver, that rest-activity, and rhythm of urinary calcium excretion both separated from the rhythms of body temperature and excretion of urinary potassium and water.

C. In addition, REM-sleep propensity and plasma cortisol concentration go along with core body temperature rhythm while rhythms of skin temperature and of plasma growth hormone concentration tend to follow the rest-activity cycle and the circadian timing of slow-wave sleep.

D. The pacemaker driving core body temperature, et al. will be labeled X while the one driving rest-activity cycle will be called Y.

E. Several physiological systems (e.g., the thermoregulator system) receive inputs from both pacemakers like the thermoregulatory system (predominantly X but some Y) and the sleep and arousal centers which receive inputs from Y, determining slow-wave sleep, while at the same time REM sleep is timed by X.

F. Most subjects in free-run studies will eventually desynchronize, but staying internally synchronized for over a month is seen (cf. figure 3).

G. These pacemakers are coupled and the coupling links between them are presumably neural or hormonal, and "act to ensure their mutual entrainment under normal conditions."

H. The coupling strengths are unequal, probably 4:1. Neither, however, is strong enough to maintain internal synchronization indefinitely in the absence of zeitgeber inputs.

I. Evidence (cf. figure 3) that coupling interactions between the pacemakers remain to some extent even after desynchronization in the form of the core body temperature rhythm modulating the sleep-wake rhythm.

J. Their lesioning studies with squirrel monkeys suggest the SCN contain (or are) the Y pacemaker and that the X pacemaker is located outside the SCN.

K. Studies in unicellular organisms have shown that single cells are capable of generating circadian rhythmicity; however, a number of observations suggest that the rhythms are secondary oscillators.

   a. Leads us to the concept of a pacemaker that coordinates a number of secondary oscillators which is supported by his studies of SCN lesions.

L. Sometimes a behavioral or even a temperature rhythm may split into two or more independently free-running components (from animal studies) which may be the result of either the secondary oscillators becoming uncoupled or, alternatively, the pacemaker itself may be composed of two components.

M. "The construct proposed here -- two major pacemaking systems presiding over populations of secondary oscillators--relies on a synthesis of data from human temporal isolation studies and animal neurophysiological experiments." Are human circadian timing systems similar to those of mammals?

a. Humans do have a SCN but it is smaller and more diffusely organized than those of other mammalian species; but there is no reason to believe that they differ in the functional role in the circadian system. Other differences noted.

8. March 1985

9. March 1985

W.H. Saris, R.A. Binkhorst, *The Use of Pedometer and Actometer in Studying Daily Physical Activity in Man. Part I: Reliability of Pedometer and Actometer,* European Journal of Applied Physiology and Occupational Physiology, Vol. 37, 219-28, 1977.

1. The article reports on a critical evaluation of the pedometer and actometer for estimating daily physical activity. The following report will focus on the actometer.

2. The participants were 6 adult males (range 21-31 years) and 9 children (range 5-6 years). The subjects were familiar with walking and running on the treadmill.

3. The actometer used is an automatically winding calendar wrist watch from which the escape mechanism has been removed causing the rotor to be directly connected to the hand. The results are read in days and hours (by conversion from actometer units). The instrument records acceleration and deceleration with a component in the same plane as the face of the watch.

4. In one part of their study, subjects wore actometers fixed to the right ankle and right wrist. The adults walked and ran at different speeds for 10 minutes. The children walked 10 minutes and ran 5 minutes. The experiments for all of speeds were repeated a second day. In another part, they ran calibration tests on the actometers, first by placing them on a carriage connected by a drive shaft with a crank rotating at different speds. The actometers were tested on a rotaing plate with their faces parallel to the plane of rotation. Secondly, with the same apparatus, the actometers were tested with the carriage moving horizontally, to and fro.

5. For the reliability testing, the results were of 10 actometers (units rotating and moving back and forth, each for 5 hours). The data collected during the tests with the subjects were readings from actometers fixed to the right ankle and right wrist taken after the subjects walked and after they ran. For the adult participants, the amount of energy expenditure was calculated using formulas presented in the text.

6. For the reliability values, the mean and standard deviation for each actometer for both rotation and horizontal movement were found, and the results from an analysis of variance per actometer and for ten actometers were done and presented. The mean and standard deviation for walking and running were presented. They also gave stride frequency numbers and plotted mean values over time (running and walking) versus energy expenditure.

7. A. Calibration

   a. For rotation, the degree of reliability obtained with the same watch was extremely high while the differences between watches were very small.

   b. With horizontal movement, the reliability of each watch was satisfactory except for one. But there were large and significant differences between the watches.

   B. Walking and Running

   a. There is an increasing number of actometer units per step with increasing speed, showing the fact that the actometer also reacts on the intensity of the movement.

   b. The results show that the counts of the actometer fixed at the ankle have a closer relation with the energy expenditure than that of the pedometer fixed to the waist. Prefer actometer to pedometer.

8. April 1985

9. May 1985

W.H. Saris, R.A. Binkhorst, *The Use of Pedometer an Actometer in Studying Daily Physical Activity in Man. Part II: Validity of Pedometer and Actometer Measuring the Daily Physical Activity,* European Journal of Applied Physiology an Occupational Physiology, Vol. 37, 229-35, 1977.

1. Article is a report of a study which monitored the physical activity in a classroom by means of a pedometer,actometer, and by observation. The intent is to determine if actometer results give a reliable estimation of activity in children.

2. Eleven kindergarten pupils, aged 4 to 6 years, were tested. The school was made-up of several classes of 20 to 30 children each. From data on the physical activity of the children (collected from an activity questionnaire completed by the infant-guides), 11 boys and girls with the highest and lowest scores were selected for the experiment.

4. Each child was fitted with A pedometer at the beginning of the schoolday. The pedometer was fixed to the child's waist at the right side. The two children with the highest and two with the lowest questionnaire scores were also fitted with an actometer which was fixed to the ankle and wrist at the right side. (Further details given.)

5. In addition to the recordings from the devices, the children were observed by someone familiar with them, and an appropriate activity category (given in text) was recorded for each child every two minutes.

6. The activity category was translated into an energy expenditure index based on a table by Bink, et al. (cf. paper). The mean and standard deviation of this factor was calculated and presented, as well as the mean and standard deviation of the pedmeter units and actometer units, both ankle and wrist. (Nowhere did they mention how the pedometer or actometer worked nor the meaning of a "unit.") They tested the above values for significance using the Student's *t*-test. They also plotted activity levels for the 4 different methods--observation index, pedometer, actometer ankle, actometer wrist--of the most and least active boys and girls.

7. A. High correlation was found between data obtained through observation and data obtained by both instruments.

   B. Pedometer underestimates physical activity of high intensity. But in a classroom, children limited in

amount of running permitted which, perhaps, hides the limitation of the pedometer.

C. The actometer on the wrist shows a smaller correlation with the other variables. Might be measuring different type of activity.

D. Observation correlates better with ankle actometer or pedometer, suggesting that the general observation method pays more attention to movements of the leg.

E. Actometer is useful in studying physical activity--need further research. Might be good to combine actometer with the more expensive instruments like the heartbeat recorder.

F. Pedometer has more limitations (in recording the intensity of an activity).

8. March 1985

9. May 1985

Wilse B. Webb, *Sleep, Biological Rhythms, Performance Research: an Introduction,* Bilogical Rhythms, Sleep, and Performance John Wiley & Sons, 1982.

1. Chapter is survey of sleep research, chronobiology, and performance research.

7. A. Sleep research, chronobiology, and performance research have developed as three separate areas, but there is (and should be) growing interplay among them.

B. Sleep Research

a. Sleep is measured in three dimensions:

i. patterns of sleep (sleep/waking relationship);

(1) Major summary variables are total sleep time, the number and length of episodes, and placement of sleep within 24-h.

(a) These are modified by age, individual differences, naps, and shift work.

ii. structure of sleep (within-sleep characteristics);

(1) Sleep structure is, for the most part, indexed by EEG. The EEG record can be reliably visually categorized in stages, each of which displays distinctive characteristics.

(a) Records are reviewed in one minute or thirty second epochs.

iii. subjective evaluation of sleep (i.e., good, deep, etc.).

(1) Gathered by questionnaire.

b. Sleep has been studied as dependent or independent variable.

i. dependent: using EEG recording, for example, to study effects of presleep exercise on sleep EEG measures, or do chemical or electrical stimulation;

ii. independent: an example is deprivation of various stages of sleep and effect on performance.

C. Biological Rhythm Research of Chronobiology

a. Studies behavior over time and biological synchrony within the organism relative to time (the more recent development).

b. "A biological rhythm can be described as a measurable change in a biological event which displays a tendency to reoccur in a systematic time schedule." This is complicated, however, by noting that such temporally ordered changes occur as a function of:

i. systematic, timed changes in the external environment (e.g., light, temperature, and learned signals);

ii. homoeostatic systems in which a depletion (or excess) results in a counter response (e.g. eating or drinking); or

iii. internal or endogenous timing systems (e.g., bird migration or the oestrus cycle) (p. 9).

c. The above get at the core of what is meant by a biological rhythm.

d. Reserach issues include the establishment of :

i. presence of rhythms--done either by transverse method (measures are taken across a fixed time span on independent subjects) or longitudinal method (measures on a single subject are repeated over time).

ii. endogenous and exogenous determinants --looking for timing sources.

(1) Must keep in mind the five major sources of behavior change which also show time characteristics:

(a) reflex responses (e.g., pupillary response to light);

(b) instinctive responses;

(c) Learned responses;

(d) homoeostatic responses that deal with the maintenance of a constant state;

(e) maturation or development changes.

(2) A mature organism in a physiologically balanced state in a constant-stimulus environment would, in a biological rhythm model, continue to display rhythmic response.

iii. Types of research designs: time-free, desynchronous, or phase change.

iv. Also much research on determining control mechanisms of rhythms (i.e., looking for the clock).

D. Performance Research

a. Four major approaches: sensory-discriminatory performance, learned performance, mental abilities measurement, and skill performance.

b. This field in the domain of psychology--extensive literature.

c. Performance research involves three general aspects: the selection of performance measures, experimental control, and data analysis.

8. February 1985

9. March 1985

2.1.3 Additional Bibliography

2.1.3.1. First Priority

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2.1.3.2 Second Priority

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2.2 Mathematical Methods

A recent review (deBoer, Karemaker, and Strackee, *Psychophysiology*, Vol. 22, No. 2, March 1985) presented a survey of techniques that transform HRV data into signals that were both visually informative and accessible for analysis. They also discussed several models that have been proposed as plausible representations of the underlying physiology. Specifically, they include an explanation for the transformation of a continuous signal into a series of events (heartbeats). They defined and compared the following measures and models:

1. Instantaneous Heart Rate (IHR): the inverse interbeat interval during the interval concerned. Contrasted with the delayed heart rate (DHR) signal, which is always one beat late.

2. Integral Pulse Frequency Modulation (IPFM) model: it is shown that when the IHR is used as an input to the IPFM model, the event series from which the signal was derived appears at the output. They take this to mean that if the IPFM is accepted as a model of the pacemaker the IHR signal may be considered as an approximation of the neural influence on the pacemaker.

3. Low Pass Filtered Event Series (LPFES): this signal is consistent with the IPFM model, and is attractive because it is a smooth function of time. It has the two disadvantages of being not easy to compute from the event-series signals, and the filter is non-causal, making it difficult to evaluate.

These approaches provide excellent features, including those that can be extracted from the spectral (frequency-domain) representation, as would be produced by a Fourier transform of the data; the features then can be used in clustering or classification algorithms.

2.3 Data Review

Data have been received from the army that describe the effectsof various doses of atropine, as represented by heart rate and activity measurements. The data were recorded for five non-contiguous days, one for each level of atropine. Actigraphy data were partitioned in 2-see intervals, and an RMS value computed for each. The R-R interval was a measure of reciprocal heart rate. The data were presented in half-hour-long files.

These data are available for two subjects, and will form the basis for our exploratory work in the early part of Year 2.

In the case of time series data, such as motor activity records, many powerful analytic techniques exist, but must be used with care. In the analysis of electroencephalograph (EEG) signals, for example, Sanderson, et al. [1980]. observes that the techniques that assume stationarity have tended to produce an oversimplified representation, while those that describe nonstationary changes yield unwieldy amounts of data. An autoregressive (AR) model does provide a predictive model of a stationary time series and has been applied to EEG (e.g., Sanderson, et al., 1980). The predictive properties of the AR model were used by Lopes da Silva, et al. [1977] to detect transient events in the EEG. The most commonly used techniques for nonstationary analysis have been based on spectral analysis; complex demodulation (Walter, 1968) has been used with nonstationary EEGs to estimate a narrow-band component, such as amplitude variation of alpha components.

Sanderson, et al. [1980] takes the approach of modeling a discrete-time signal using a piecewise stationary stochastic sequence. Central to the method is a test for departure of observations from a time series model, developed by Segen and Sanderson, [1980].

If the observed sequence is $\{x_n\}$, the test (Sanderson, et al., 1980) begins by transforming $\{x_n\}$ into a sequence $\{v_n\}$ defined by

$$U_n = \left(\int \sum_{i=1}^{n} f(x|x^{i-1}) \log f(x|x^{i-1}) dx - \log f(x_i|x^{i-1}) \right),$$

where

$$f(x_n|x_{n-1}, x_{n-2} \ldots, x_{n-p}) \triangleq f(x_n|x^{n-1}).$$

The following properties of the transformed seqeunce U_n were shown in Segen and Sanderson [1980]:

1. As long as x_n remains stationary, the mean of U_n is 0, and U_n behaves approximately as (converges in distribution to) a Weiner process.

2. After the change, the U_n behaves approximately as a Weiner process with a constant, positive drift.

Based on these properties of U_n, a fixed sample size test for change was proposed in Segen and Sanderson [1980]. The test uses a statistic,

$$R_n = \max_{i<n} (n^{-\frac{1}{2}} \sigma^{-1} U_n)$$

where

$$\sigma^2 = \text{var}[f(x|x^{n-1}) \log f(x|x^{n-1}) dx - \log f(x_n|x^{n-1})].$$

The limiting distribution of R_n is given by

$$\lim_{n\to\infty} \Pr(R_n \leq \alpha) = 2(2\pi)^{-\frac{1}{2}} \int_0^{\alpha} e^{-x^2/2}\, dx \qquad (1)$$

The test outlined above is applicable to any predictive model of the process, and several examples are discussed in Segen and Sanderson [1980]. An important property of this test is that the parameter α in (1) provides a detection threshold which is directly interpretible in terms of the statistical significance of the test. Thus, by utilizing the transformed process U_n, a fixed sample size test is developed directly which, for a given significance level, does not require the specification of any arbitrary parameters.

For application to the segmentation of EEG signals, we have chosen to utilize an autoregressive model for the signal. For an autoregressive process

$$x_n = a_1 x_{n-1} + a_2 x_{n-2} + \ldots + a_p x_{n-p} + v_n \,,$$

R_n becomes

$$R_n = \max_{i<n} \left[(2n)^{\frac{1}{2}} \sum_{k=1}^{i} \left(\frac{e_k}{\sigma^2} - 1 \right) \right] \qquad (2)$$

where e_K is the one-step prediction error and

$\sigma^2 = E(v_n^2)$.

The segmentation procedure applied to the EEG signal consists of the following steps:

1. Parameters of AR model are estimated from the initial k values of the signal using the recursive algorithm of a Bayesian estimator (Kashyap, Rao, 1976).

2. The statistic R_n given by (2) is computed for n=10, 20, 50,and 100, beginning at k+1, k+2, k+3... and tested for increase above α. The values of α are calculated from (1) for a given significance. The negative thresholds are also set to detect a decrease of the variance.

3. Parameters of a new model are estimated from the k values following the detection point and the time of the change is determined more accurately by adjusting backwards for the minimum total variance of the residuals of the two models. The procedure returns to step 2.

The procedure described above results in a series of AR models, each corresponding to one time segment of the EEG signal. Use of the recursive estimation of the autoregressive parameters (Kashyap, Rao 1976) makes the procedure efficient and provides a more stable estimate for small numbers of samples than other techniques. This stable estimate is essential to the

reliable detection of change. The procedure which was implemented adapted a formal test derived for detection of a single change to the detection of multiple changes.

An example of the application of the segmentation procedure to a test signal is shown in Fig. 2. The signal consisted of alternating segments of sinewaves with frequencies 3 Hz and 6 Hz, amplitude 1 and length 4 s, sampled at 100 Hz, with added white noise having standard deviation 0.25. Fig. 2 shows the resulting segmentation and the plot of R_{100}. An example of segmentation of an EEG record is shown in Fig. 3. The EEG signal is from a single electrode over the occipital area of a normal adult male. The record was sampled at 100 Hz. A tenth-order AR model was estimated from 100 initial values of each segment and the significance level was chosen 0.01. In a 320 s record the procedure discovered 94 segments.

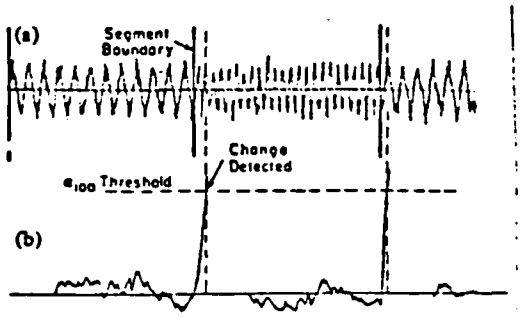

Fig. 2 Segmentation of a test signal consisting of alternating segments of sine waves with added white noise. (a) Segmented signal. (b) Plot of the R_{100} error process with threshold.

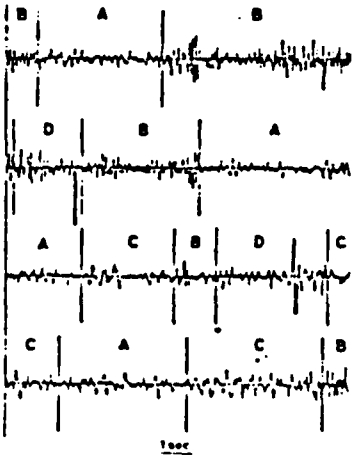

Fig. 3 Segmentation of the EEG signal recorded from the occipital area of a normal male adult.

2.3.1 Data Review References

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3. PLANS FOR YEAR 2

We intend to continue our critical review of the literature, extending it to actigraphy, the study of additional drug effects, and sleep-deprevation studies.

Data analysis will proceed as indicated in Section 2, with segmentation (especially for sleep staging) receiving much of the effort initially. This will be done without knowledge of the true state and thus will yield a conservative estimate of the performance of our methods.

An ancillary study (on man-machine interaction) being conducted separately at George Washington University will provide data that will allow much greater understanding of actigraphy as a tool; specifically, 1- vs. 3-axis comparisons, calibration accuracy and repeatability, value of RMS as compared to point-by-point measures, and ability to measure low-level activity.

4. SUMMARY

Progress is being made toward the understanding of the relationship between performance and heart-rate/actigraphy measures. Precautions are being developed that will alert us to the possible presence of confounding environmental and physiological variables. The data-analysis tools have been assembled, and the data are in a form that permits easy manipulation. We believe that substantial results will emerge during the next year.

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